

CRITICAL POINTS IN RANDOMIZED RESEARCH ON DCD DONOR IN-SITU PERFUSION (NRP): THE INTERIM DONARE STUDY CLINICAL EVALUATION

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BACKGROUND AND RATIONAL

- Controlled DCD organ donation (cDCD) is a strategic target for the Italian transplantation network.
- Italian peculiarities in cDCD donation raise concern over organ ischemic damage.
- To counter the risk of ischemic damage linked to regulatory obligations on the assessment of death **Normothermic regional perfusion (NRP)** has been strongly recommended in potential cDCD donors.
- **NRP** has been shown to be the most effective method of preservation and functional evaluation of abdominal organs in DCD donors

?
To date, it is not known whether:
➤ the inflammatory response changes during NRP and
➤ there is an association with the suitability of the organs removed

2018

DONARE study was designed to describe ischemic-reperfusion and inflammatory biomarkers during **NRP** and to assess the potential benefit of apheresis by an adsorbent filter (Cytosorb®) included in the NRP circuit

The DONARE study protocol was defined by the **DCD national working group**
Coordinated by CNT and proposed to **ALL THE ITALIAN DCD DONATION CENTERS**



2019

...after a long approval process by the coordinating center Ethics Committee and then a long process for approval in the centers followed

Participating centers

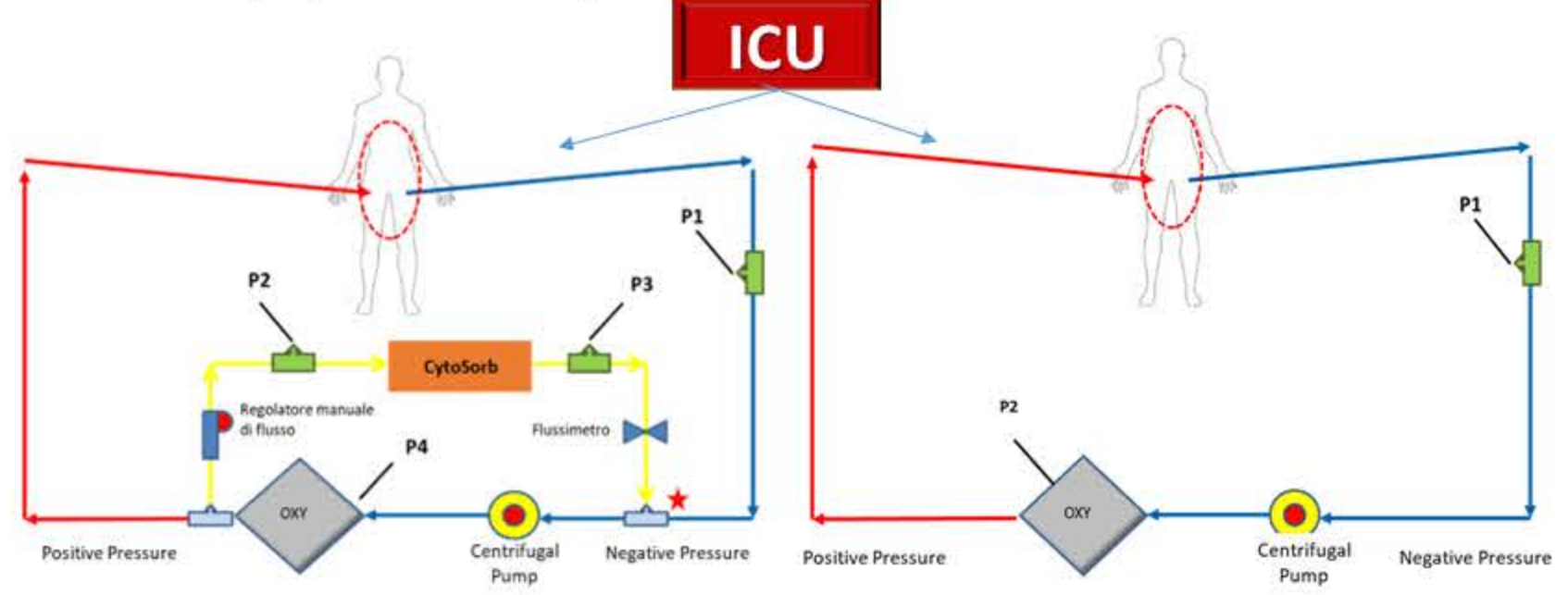
LOMBARDIA	1. Milano Ospedale San Raffaele 2. Policlinico Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico di Milano 3. Milano Niguarda ASST Grande Ospedale Metropolitano Niguarda 4. Milano S.Paolo Milano ASST Santi Paolo e Carlo, Presidio San Paolo 5. Milano Legnano 6. Pavia IRCCS San Matteo 7. Varese Circolo-Fondazione Macchi 8. Bergamo ASST Papa Giovanni XXIII → Pending approval 9. Brescia ASST Spedali Civili di Brescia → Pending approval 10. Como Ospedale Sant'Anna
PIEMONTE	1. Ospedale San Giovanni Bosco – ASL città di Torino 2. Ospedale Molinette – AOU Città della Salute e della Scienza di Torino
EMILIA ROMAGNA	1. Ospedale di Cesena 2. Ospedale di Baggiogvara
SICILIA	1. Palermo ISMETT → Pending approval 2. Cívico Palermo → Pending approval

2020

Start of the DONARE STUDY enrollment phase

The DONARE study protocol

CENTRALIZED RANDOMIZATION
CNT
40 Subjects randomly assign to 2 groups of treatments: with and without an adsorbent filter (Cytosorb®) included in the NRP circuit



DATA COLLECTION: T0 – T4

ICU

Subject #	T0	T1	T2	T3	T4
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

Laboratory for Cytokine Dosage

Samples have been blindly centralized to an independent laboratory for cytokines profiling

Serial samples (4/2 with/without Cytosorb®, from T0 to T4) in different points of the NRP circuit

CNT
OVERALL DATA COLLECTION

OBJECTIVE

The **AIM** of this work is to describe the **modulation of the clinical characteristics** and of the NRP in the **DONARE study enrolled cases**

METHODS

The coordinating center (**CNT**) has **monitored** the evolving cDCD activity to preserve the study capacity of representing the Italian scenario

RESULTS

- (1) **Main causes of exclusion among potential cDCD donors were: age above 65 (in 2020)**
At that time, the average age of DCDs in Italy was 70 and 20% of DCDs were 75 and older

Study Period	N	Subject mean Age (years)	Italian DCD Age (years)
Sept 2020 – April 2021	8	57 ± 5.9	70
AMENDMENT to the protocol: NO MAXIMUM AGE LIMIT			
2021 (May-Dec)	11	61 ± 9.0	
2022 (Jan – Aug)	17	65,5 ± 10.8	

2021

(2) **ENROLLMENT AT 31/8/2022**

All the enrolled cases became utilized donors

Utilized organ donors

	Kidney	Liver	Lung
68%	97%	10%	

LOMBARDIA
Centers: 4
Enrolled cases: **17**

EMILIA ROMAGNA
Centers: 2; Enrolled cases: **14**

Safety → No study-related adverse event has been reported

(4) **Serial samples have been completed throughout the procedure in all the cases**

BLOOD FLOW (mL/min)	T0		T4	
	Mean	StdDev	Mean	StdDev
	3005,8	811,0	2327,3	685,6
	min	800,0	700,0	2,8
	Max	4500,0	3400,0	45,0

LACTATES (mmol/l)	T0		T4	
	Mean	StdDev	Mean	StdDev
	11,2	1,7	8,1	8,8
	min	8,8	2,8	2,8
	Max	14,7	45,0	45,0

Feasibility ←

Preliminary results of comparison analysis (only first 25 cases). Examples of Cytokine (IL-6) and Lactate levels in intervention and control groups (mean and StdDev) at a sampling point (P1)

(3) **EVOLUTION NRP DURATION (minutes)**

Mean NRP duration	YEAR	Mean ±StdDv	min	MAX
decreased	2020	223 ±39.2	203	282
from 223±39,2 in 2020 to	2021	186 ±32.2	151	240
177±33,8 min. in 2022	2022	177 ±33.8	84	210

CONCLUSIONS

Coordination of multicenter studies in the **rapidly evolving scenario of controlled DCD** donation should take advantage of **continuous monitoring of real-life procedures** and **auditing of adherence to operational recommendations**.

The interim evaluation confirms the feasibility and safety of the study.